CKD: The Gap Between Epidemiologists & Nephrologists

Damanhour Annual Meeting 2013

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Professor of Nephrology,Sheffield Kidney Institute
Chairman, Global Kidney Academy
Sheffield, UK

CKD versus C-K-D:
The Gap between Epidemiologists and Nephrologists

Epidemiologists **V** *Clinical Nephrologists*

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CKD versus C-K-D:

The Gap between Epidemiologists and Nephrologists

Epidemiologists

Computerised Databases

What can I LEARN from you?

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CKD versus C-K-D:

The Gap between Epidemiologists and Nephrologists

Clinical Nephrologists

What can I DO for My Patient?

CKD versus C-K-D:

The Gap between Epidemiologists and Nephrologists

Epidemiologists | *Clinical Nephrologists*

Global Epidemic of CKD

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50%
15%
10
%
5%
Epidemiology
CKD
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CKD versus C-K-D:
The Gap between Epidemiologists and Nephrologists

Epidemiologists

Global Epidemic of CKD

Clinical Nephrologists

What is the Evidence?

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US Population CKD Prevalence

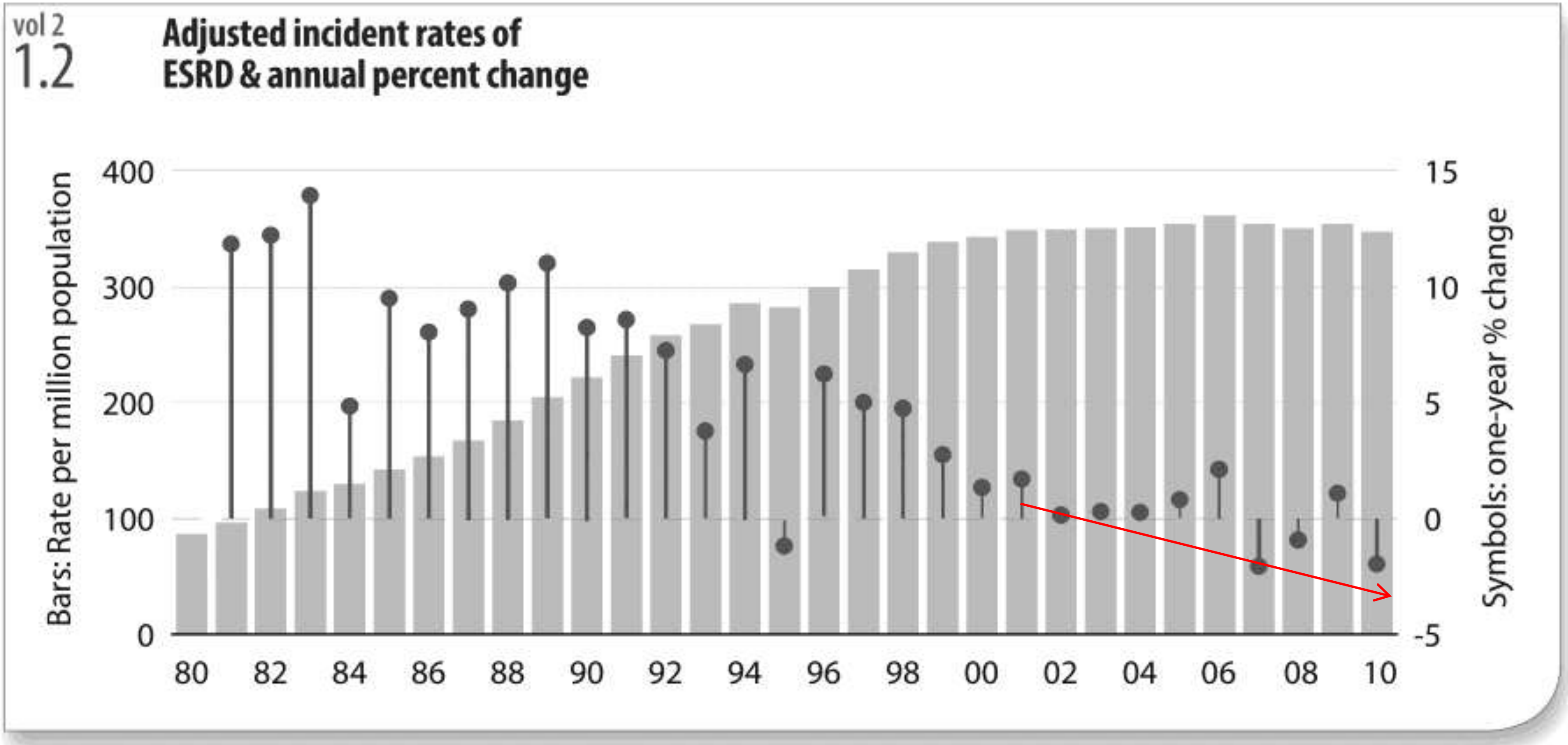
Stage/Category	%	number
1 GFR:>90	3.3	5.9 millions
2 89-60	3	5.3 millions
3 59-30	4.3	7.6
4 29-15	0.25	400,000
5 <15	0.2	345,000
Total	**11**	**19.2millions**

CKD

ESRD

ESRD UK: 842/million

Incidence of ESRD US
USRDS 2012



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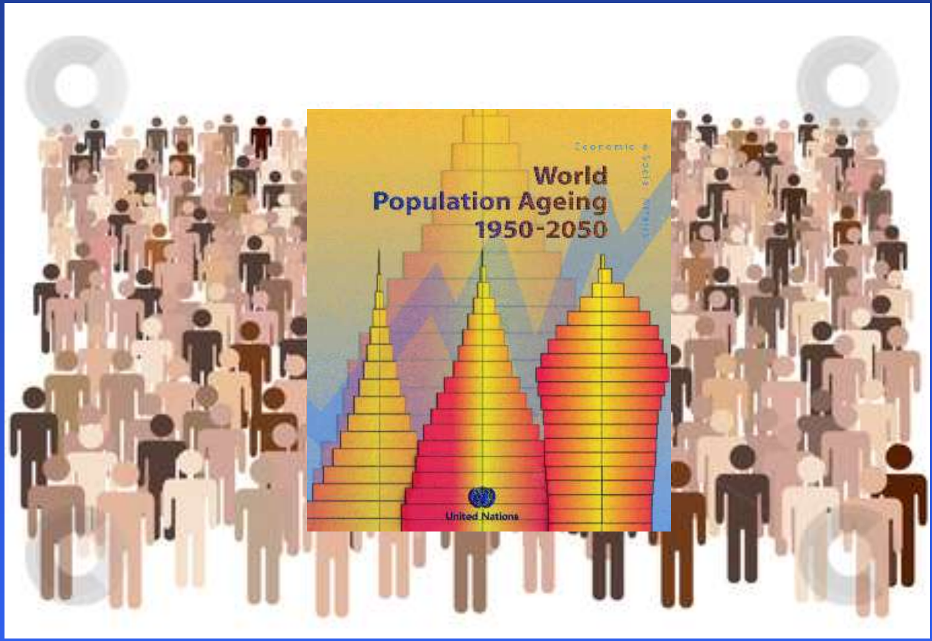
cCKD Epidemiology



cCKD = Older People

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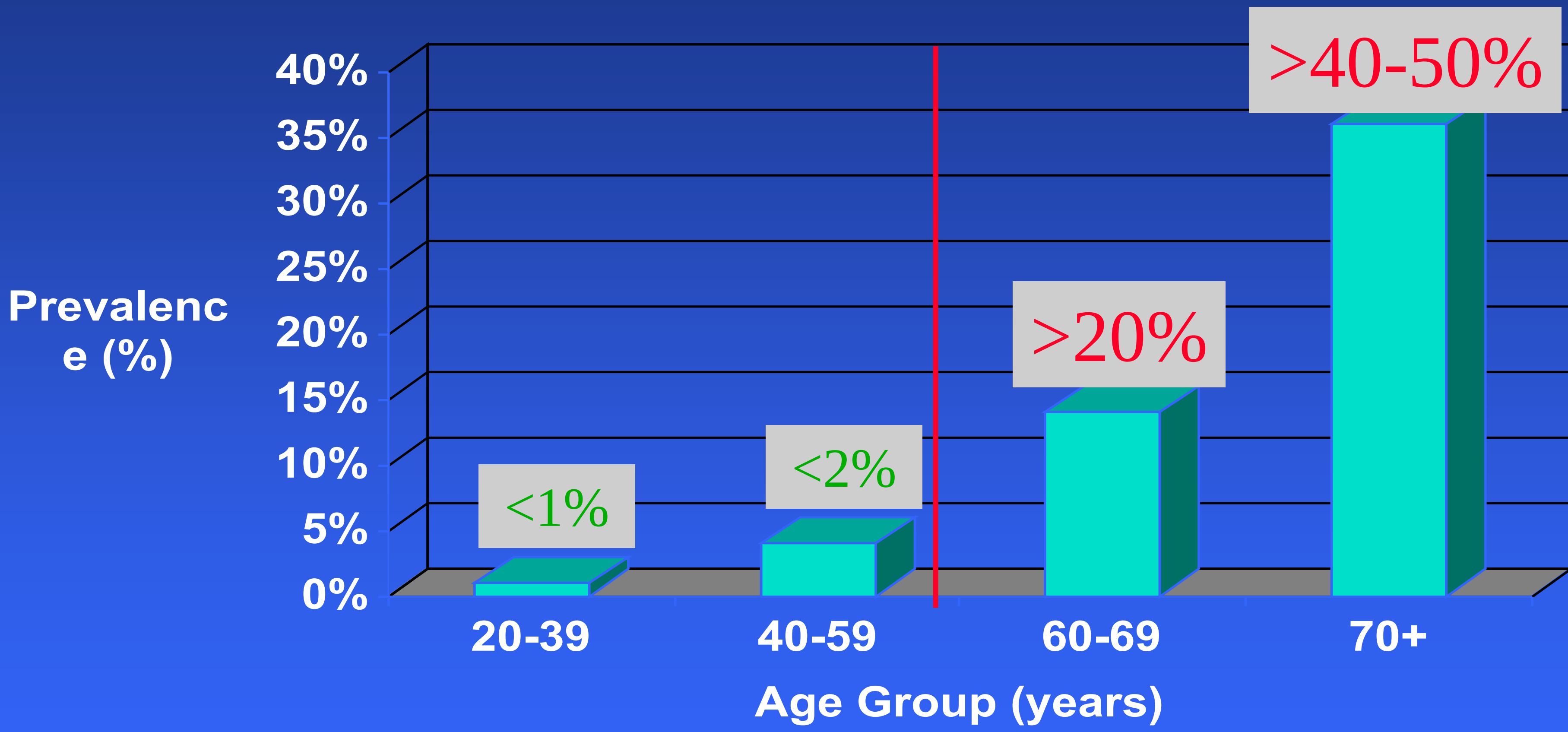
Prevalence of CKD

USA



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NEOERICA UK

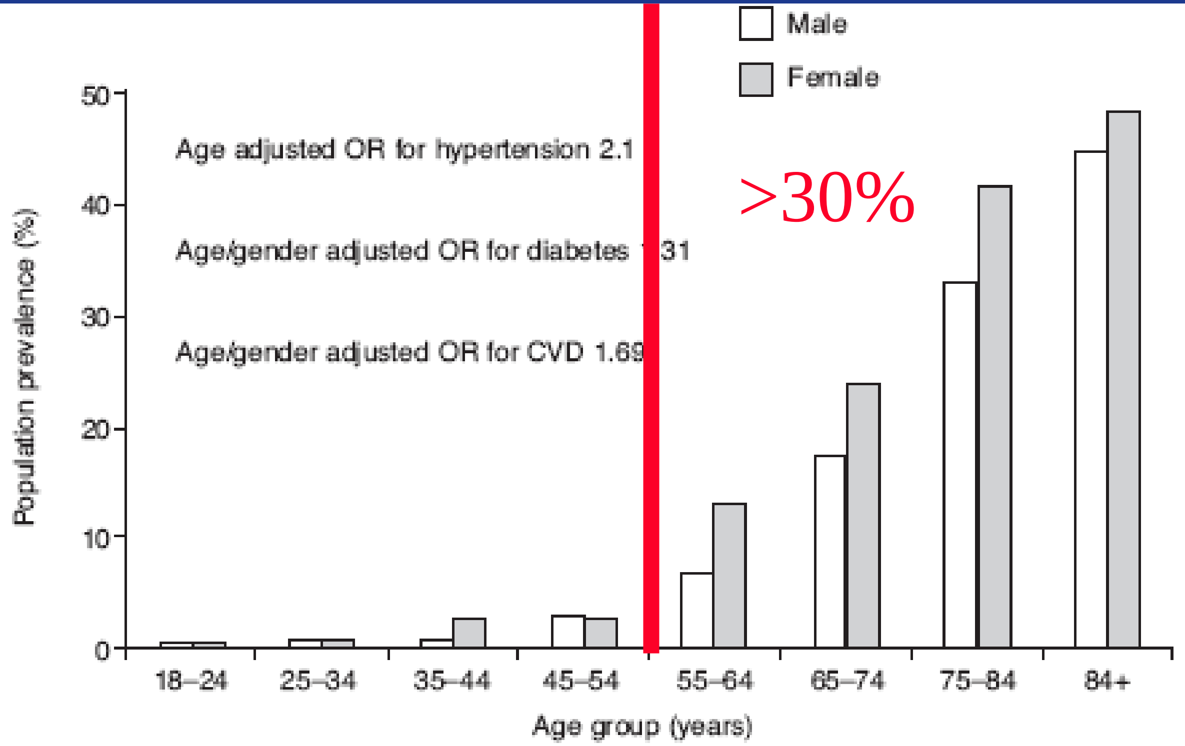

Figure 1.3 Adult CKD prevalence in the UK: age-standardised prevalence of stage 3–5 ≃ 8.5%. (Reprinted by permission from Macmillan Publishers Ltd: *Kidney International* (Stevens PE, O'Donoghue DJ, de Lusignan S et al. Chronic kidney disease management in the United Kingdom: NEOERICA project results. *Kidney International* 2007; 72(1):92–99).[19] Copyright 2007.)

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Stevens et al, 2007

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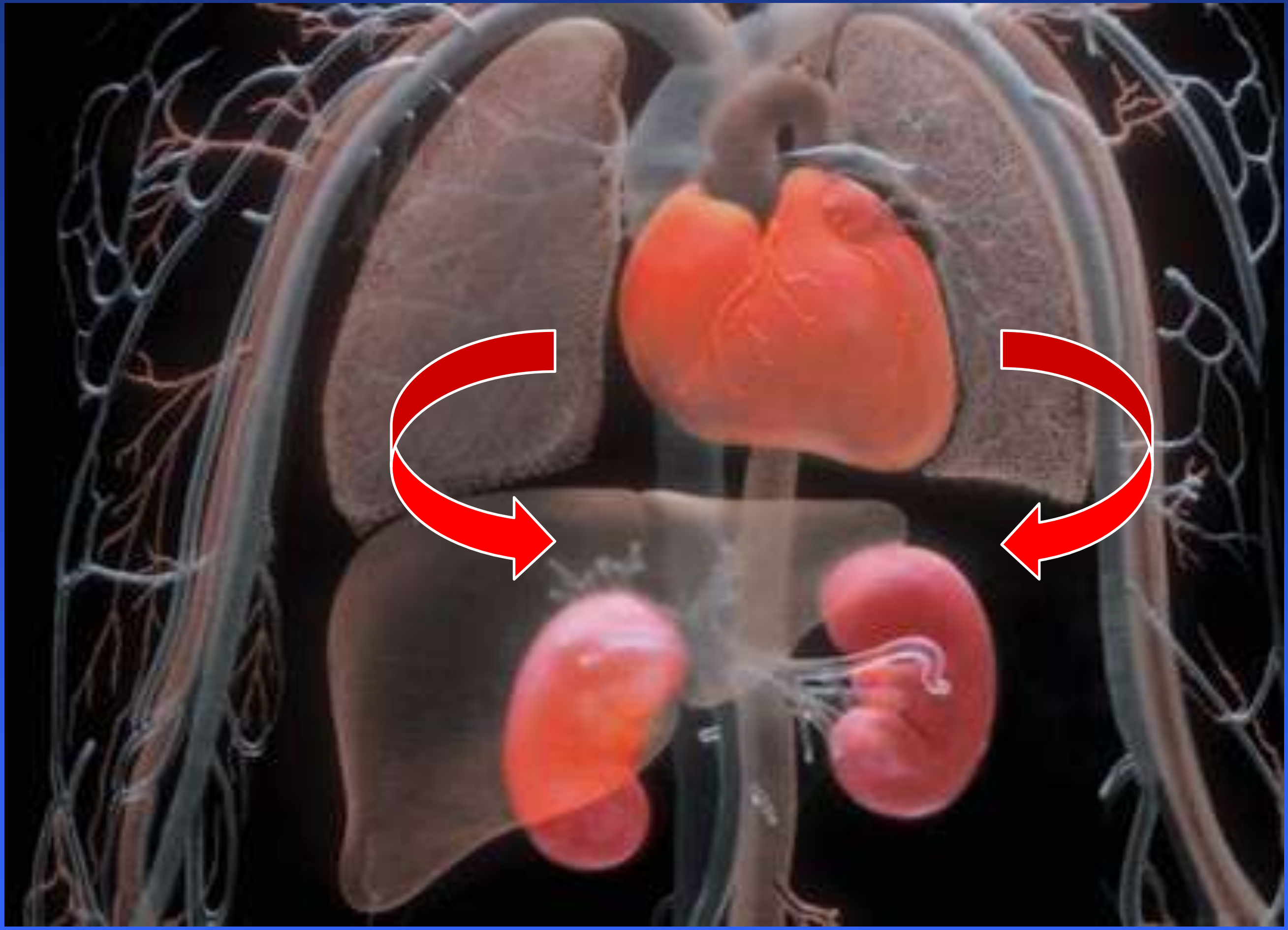
Incident cCKD and Underlying CVD



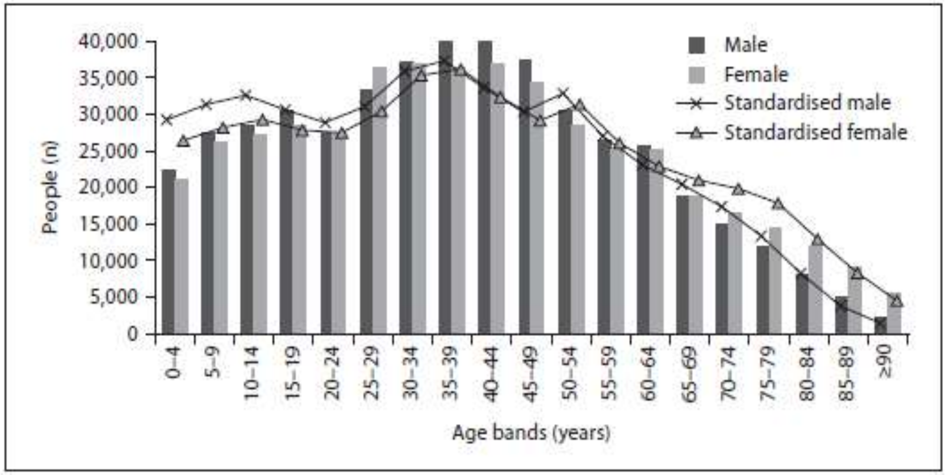
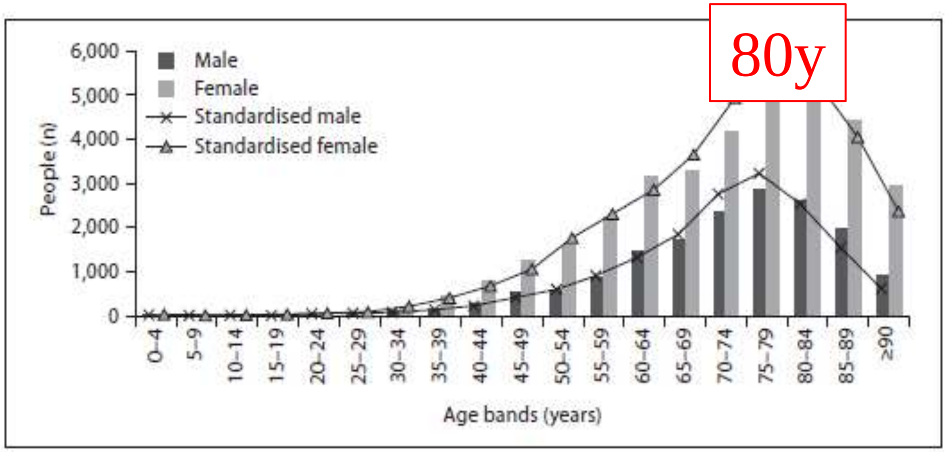


Fig. 1. Age and sex distribution of the study population (n = 930,997); lines show the standard English population (National Statistics, UK census 2001).



70% have CVD

Fig. 2. Age and sex distribution of the population with stage 3–5 CKD (n = 50,331); lines show the standard English population (National Statistics, UK census 2001).

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De Lusignan et al, 2011

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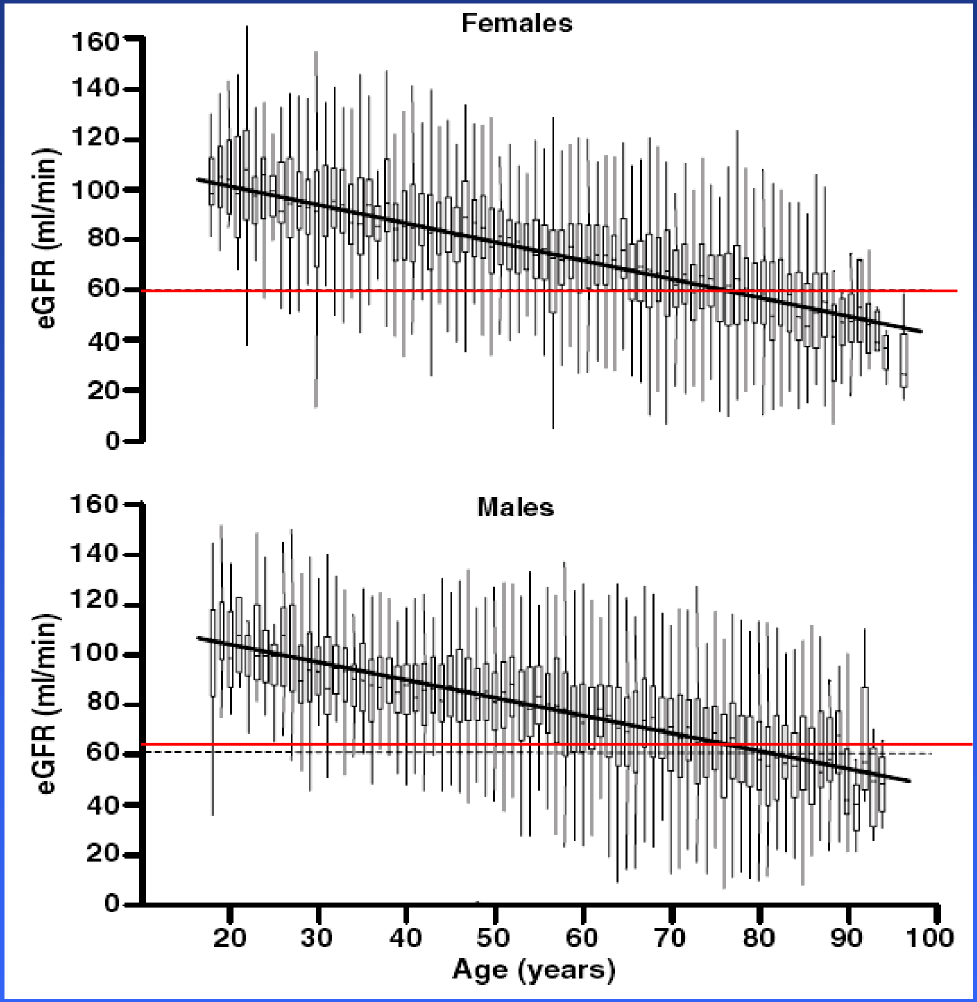
eGFR Decline with Age



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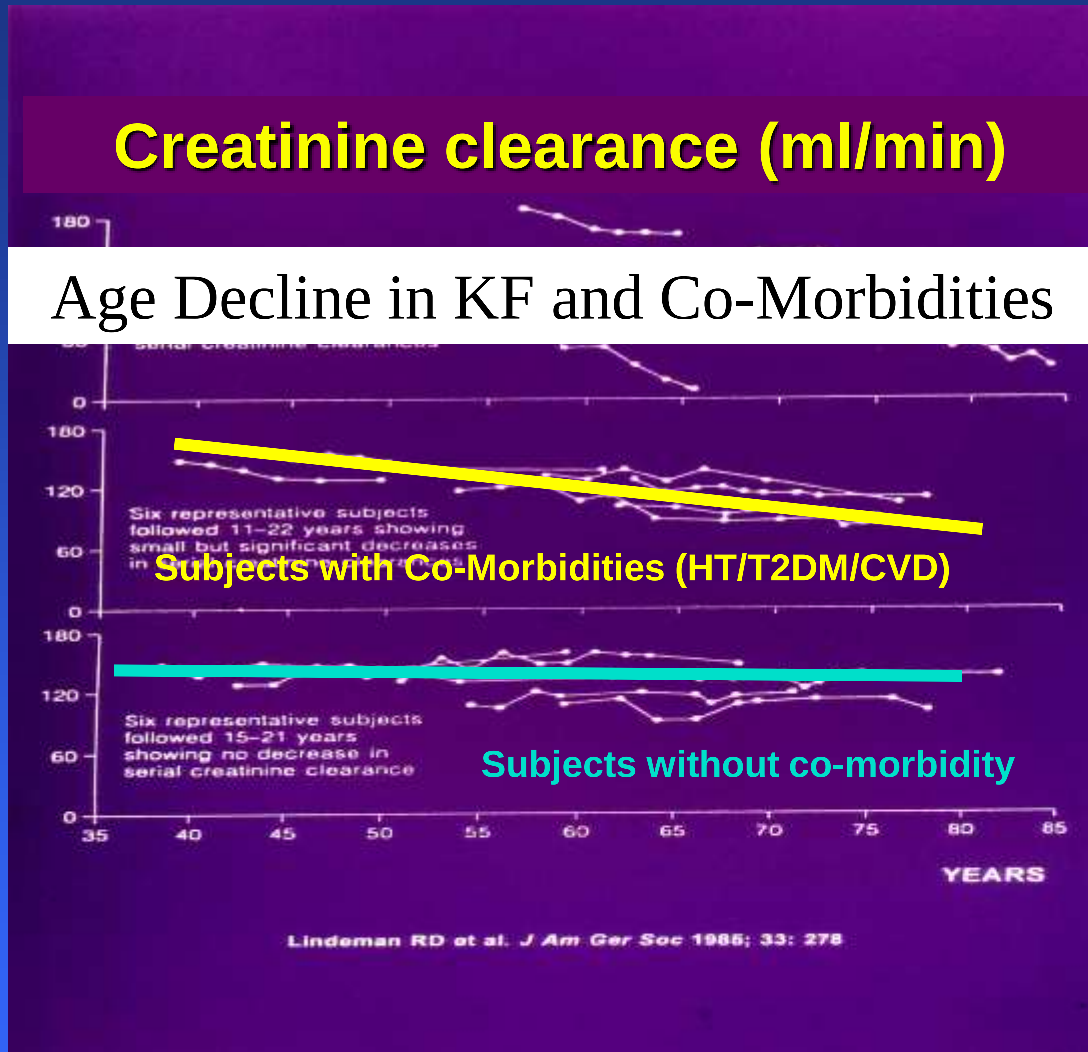
Baltimore Longitudinal Study of Ageing



Lindemann, 1985

Progression of cCKD and Sub-Clinical CVD

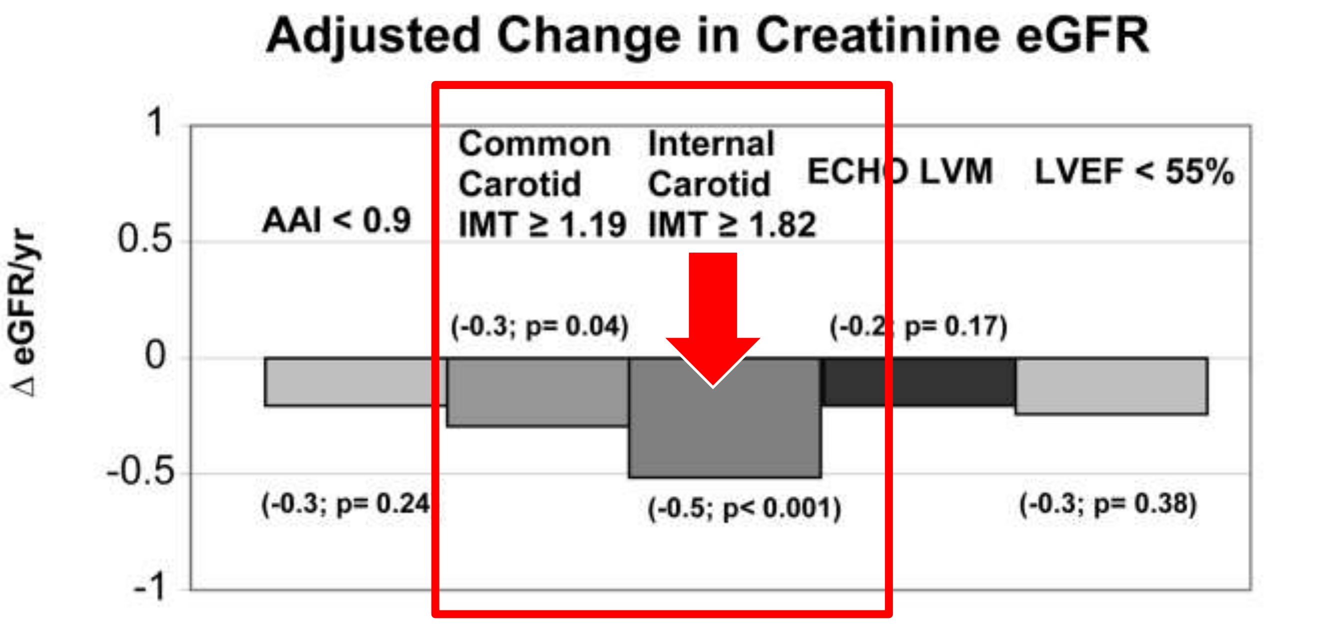


Figure 2.
Association of Subclinical Cardiovascular Disease Measures with Kidney Function Decline

Shlipak et al, 2009

Progression of cCKD and Overt CVD

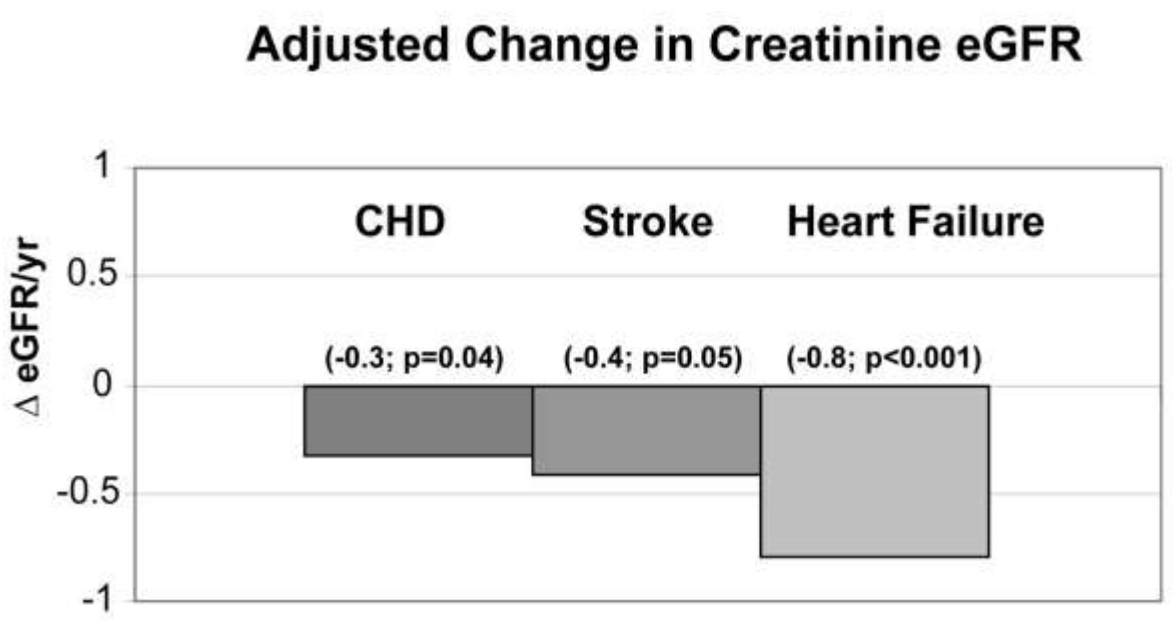


Figure 1.
Association of Clinical Cardiovascular Disease with Kidney Function Decline

Shlipak et al, 2009

Risk of developing cCKD with Ageing

Simplified Categorical Model[f]				
Age, y				
50-59	0.63 (0.12)	1.9 (1.5-2.4)	<.001	1
60-69	1.33 (0.12)	3.8 (3.0-4.8)	<.001	2
≥70	1.46 (0.14)	4.3 (3.3-5.6)	<.001	3
Female sex	0.13 (0.07)	1.1 (1.0-1.3)	.05	1
A[illegible]	0.48 (0.20)	1.6 (1.1-2.4)	.02	1
Hypertension	0.55 (0.07)	1.7 (1.5-2.0)	<.001	1
Diabetes mellitus	0.33 (0.10)	1.4 (1.2-1.7)	<.001	1
History of cardiovascular disease	0.26 (0.10)	1.3 (1.1-1.6)	.009	1
History of heart failure[d]	0.50 (0.25)	1.6 (1.0-2.7)	.04	1
Peripheral vascular disease (circulation problem in legs)	0.41 (0.13)	1.5 (1.2-1.9)	.002	1

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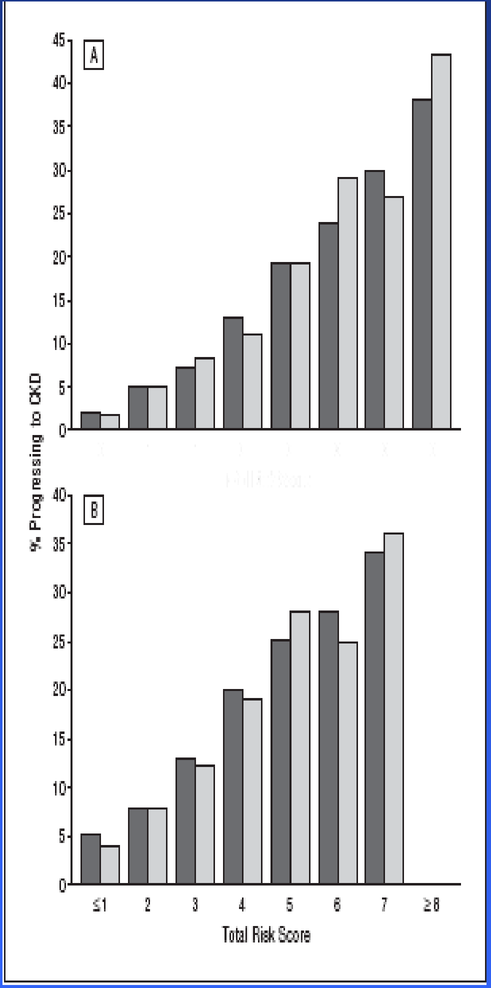
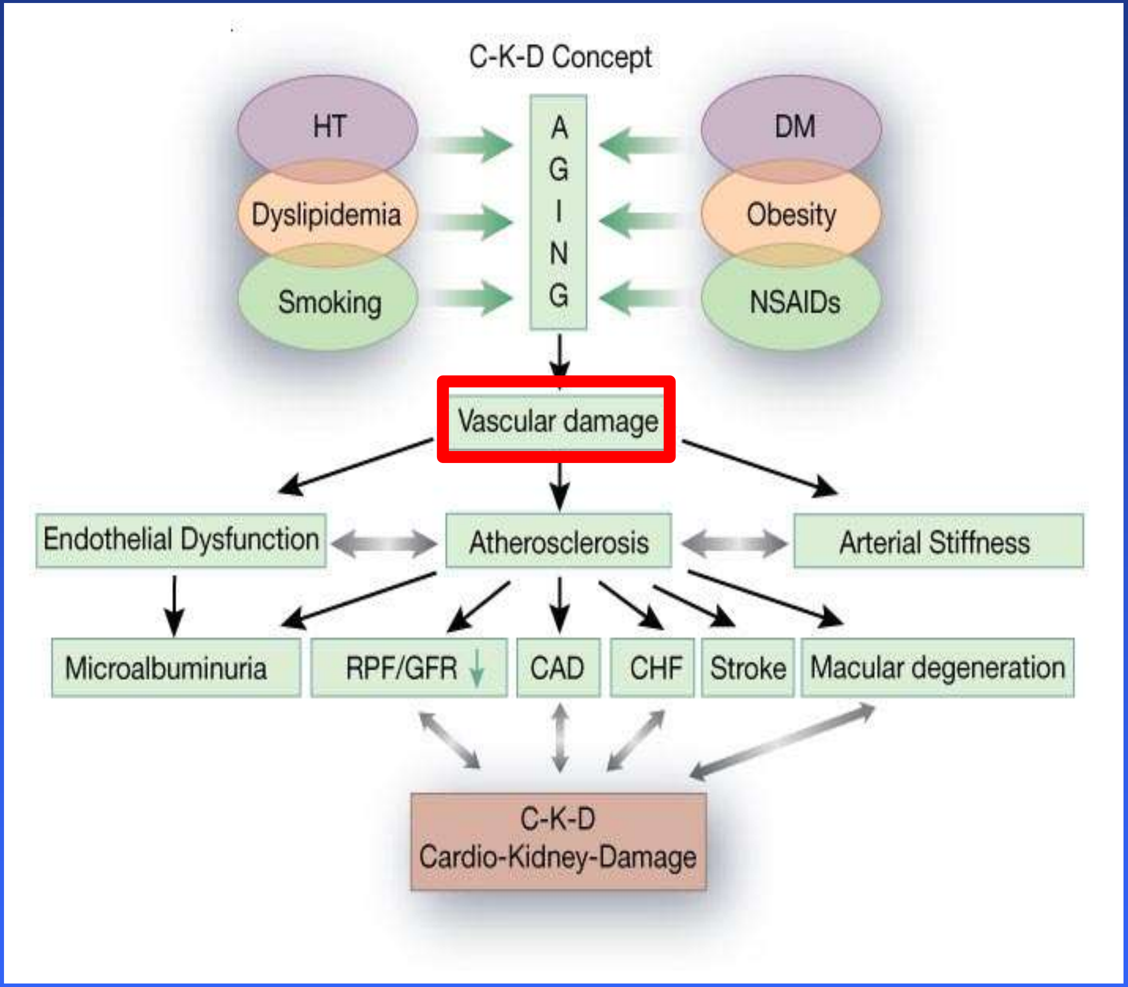


Kshirsagar et al, 2008

Atherosclerosis and cCKD



El Nahas, KI 2010

CKD versus C-K-D:
The Gap between Epidemiologists and Nephrologists

Epidemiologists

Global Epidemic of CKD

Clinical Nephrologists

C-K-D = Older People
with impaired Kidney Function

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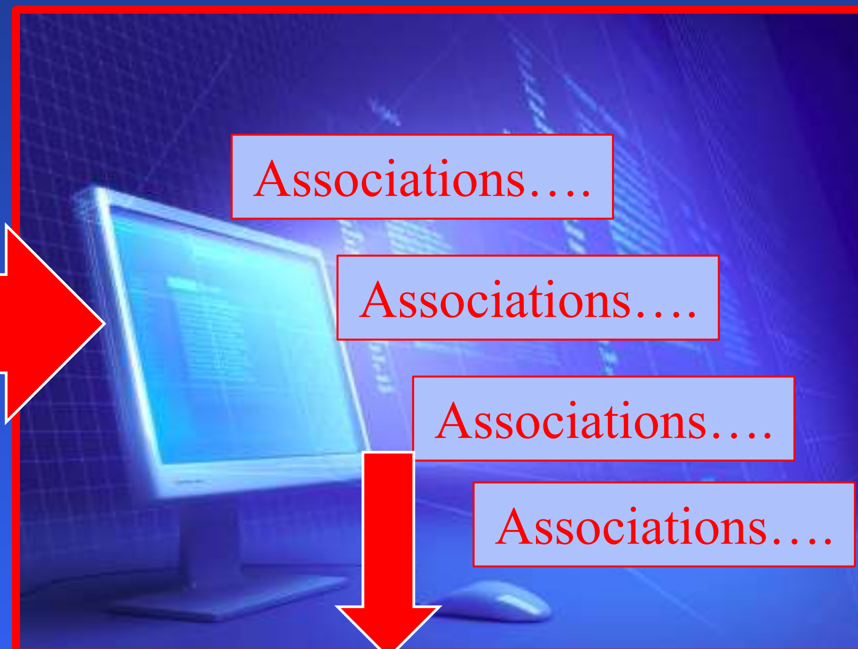
CKD : Predictor of CVD Risk

Epidemiologists

Computerised Databases



CVD

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CKD and Mortality Risk

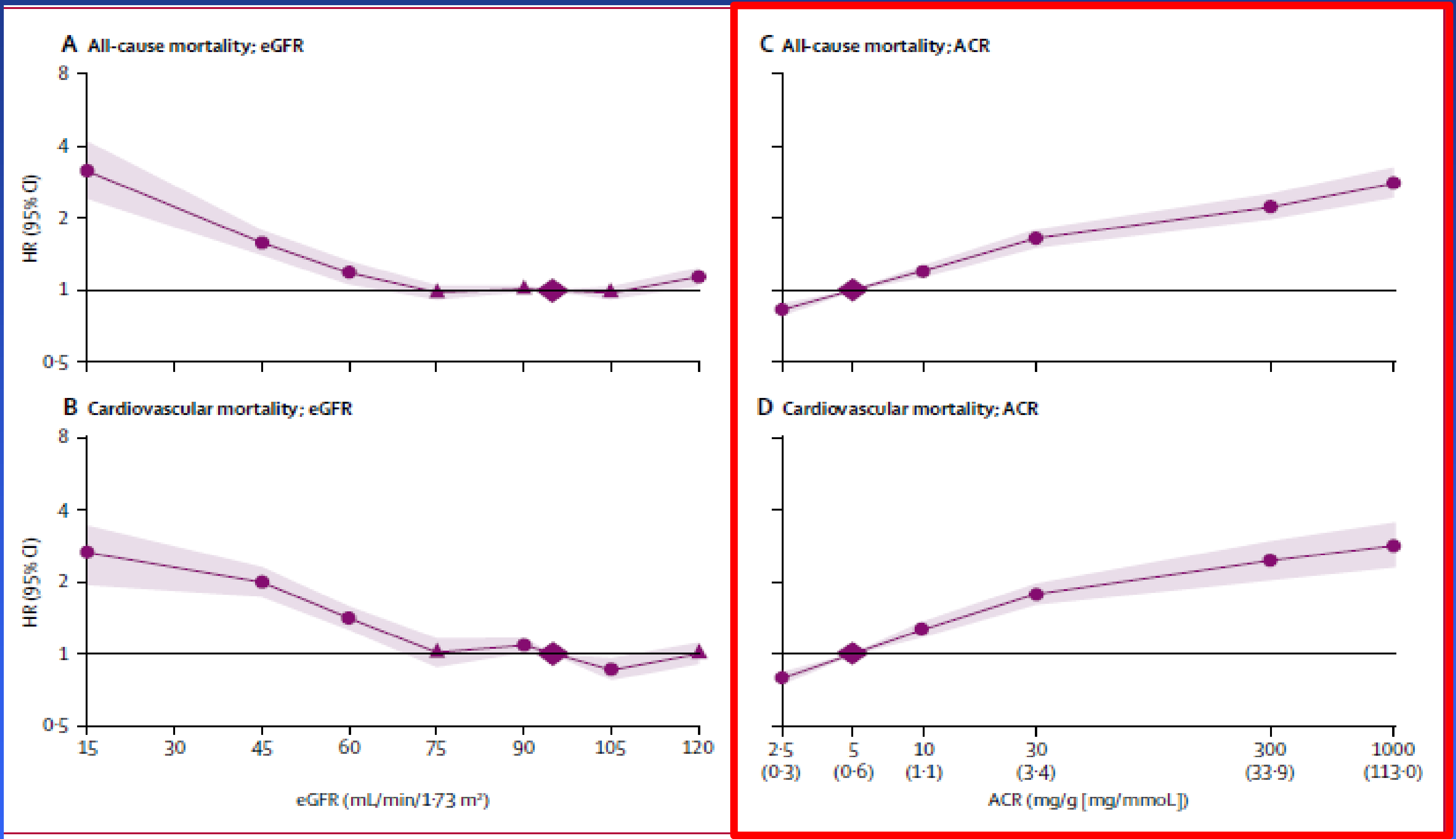
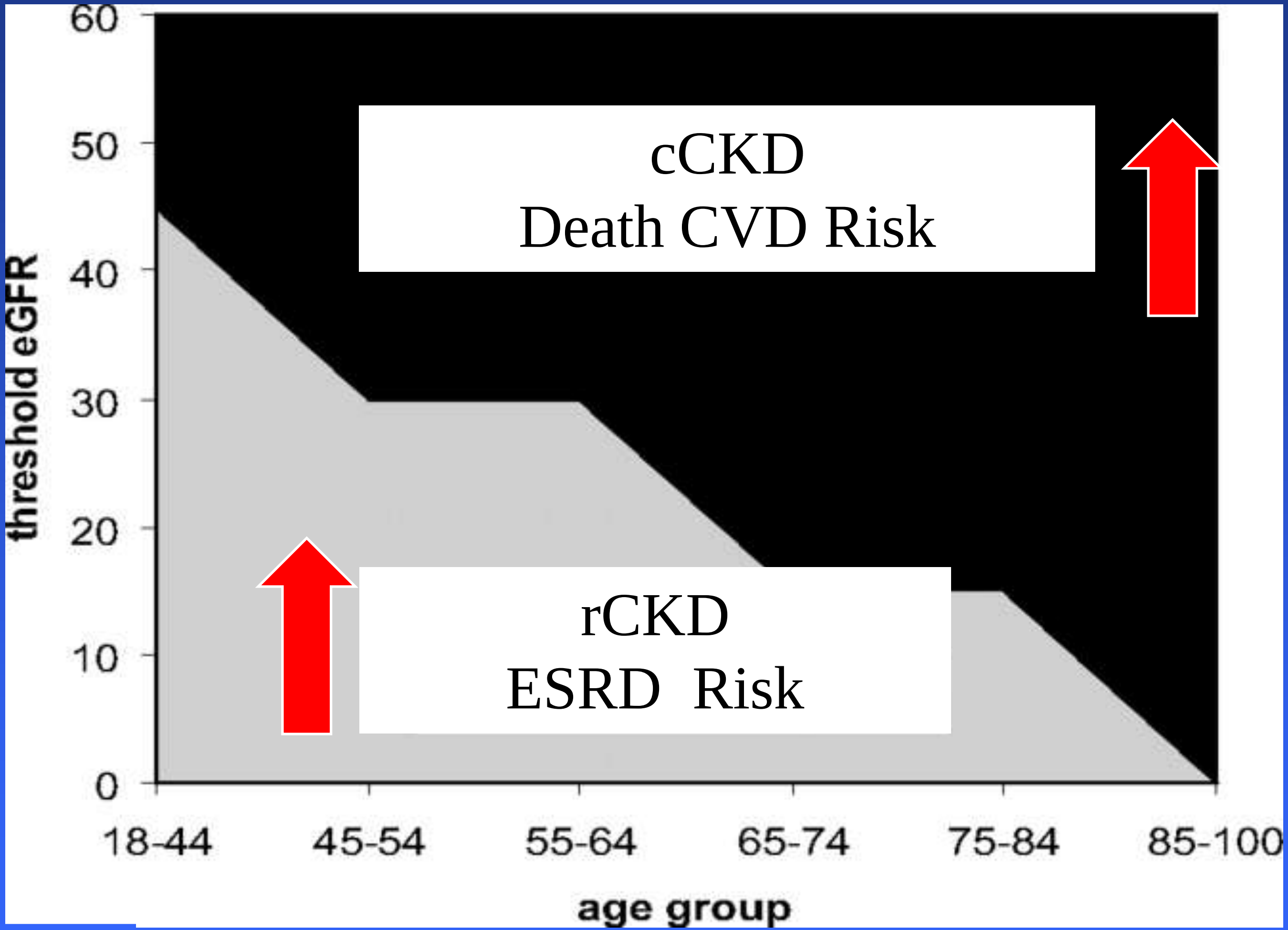


Figure 2: Hazard ratios and 95% CIs for all-cause and cardiovascular mortality according to spline estimated glomerular filtration rate (eGFR) and albumin-to-creatinine ratio (ACR)

CKD Consortium, Lancet 2010

Age impacts on outcomes in CKD

210,000 subjects, eGFR<60mls/minute/1.73m², outcomes at 3.5 years



O' Hare A et al. 2007

CKD : Value as Risk Predictor

Clinical Nephrologists

So…C-K-D = "disease" of old people with CVD
Who die from…CVD…!!!!

CKD : Value as Risk Predictor

Epidemiologists

Clinical Nephrologists

CKD Predicts RISK

What is the EVIDENCE?

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CKD and Mortality Risk

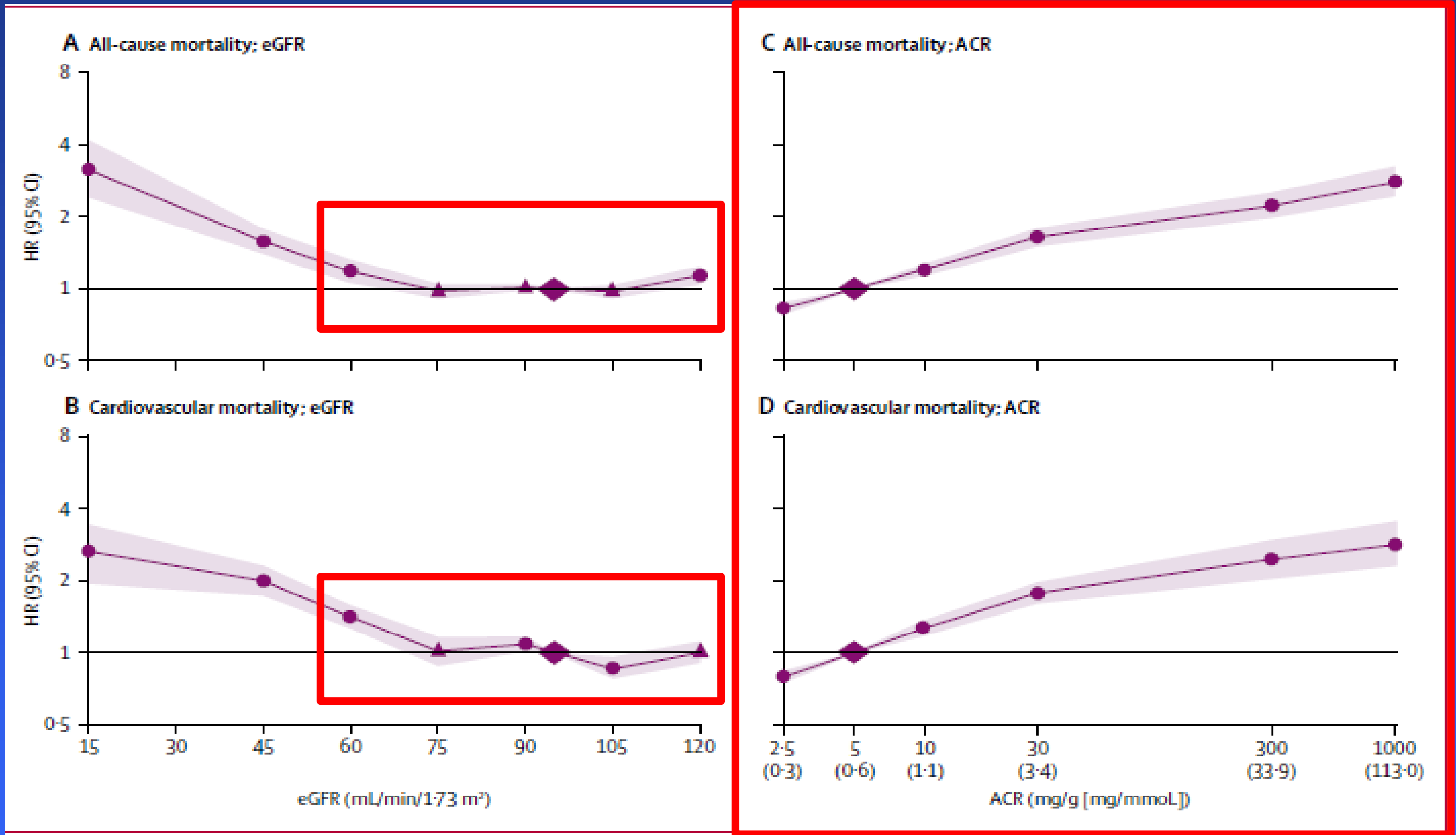
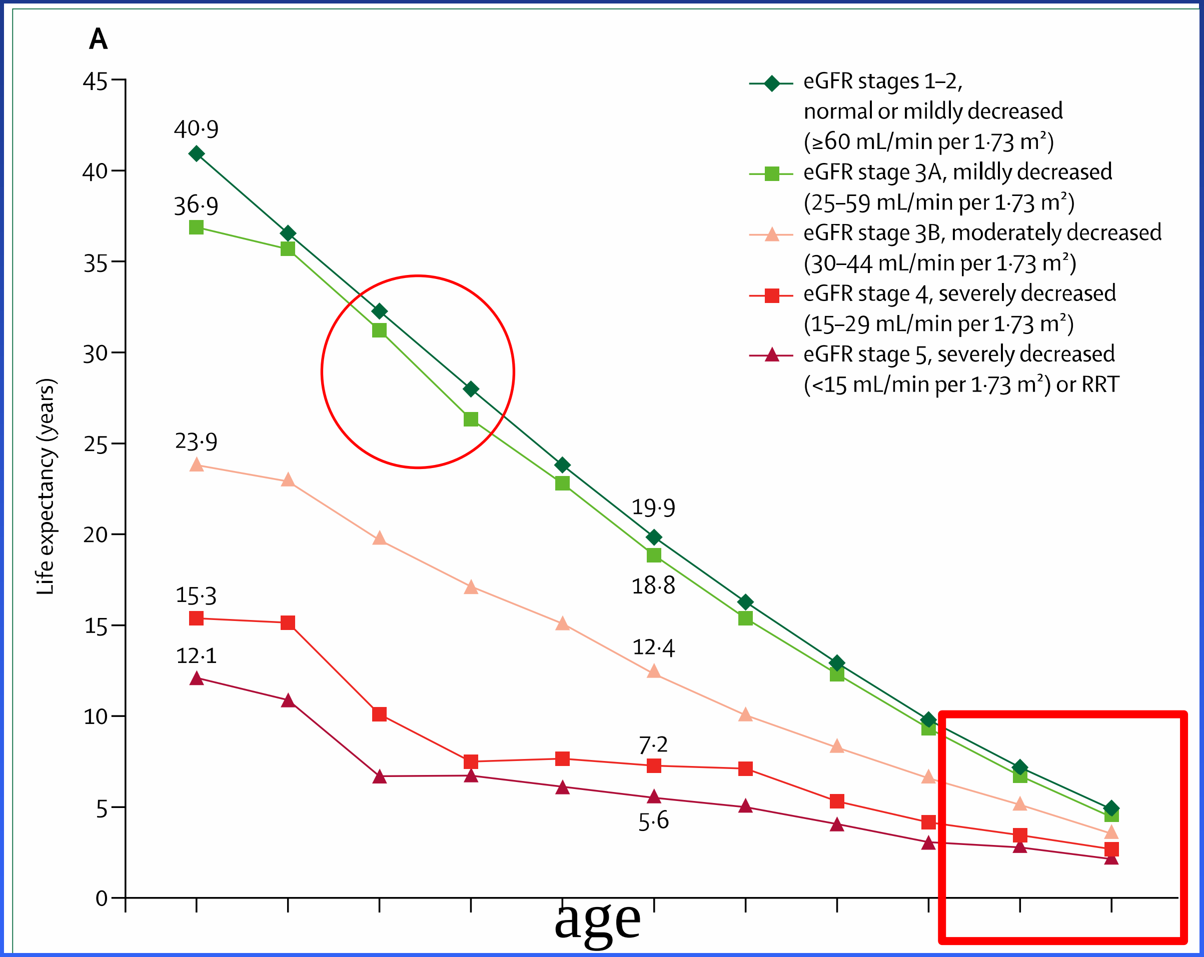


Figure 2: Hazard ratios and 95% CIs for all-cause and cardiovascular mortality according to spline estimated glomerular filtration rate (eGFR) and albumin-to-creatinine ratio (ACR)

Lancet 2010

Life Expectancy and eGFR



Gansevoort et al, 2013

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Chronic Kidney Disease Prognosis Consortium*

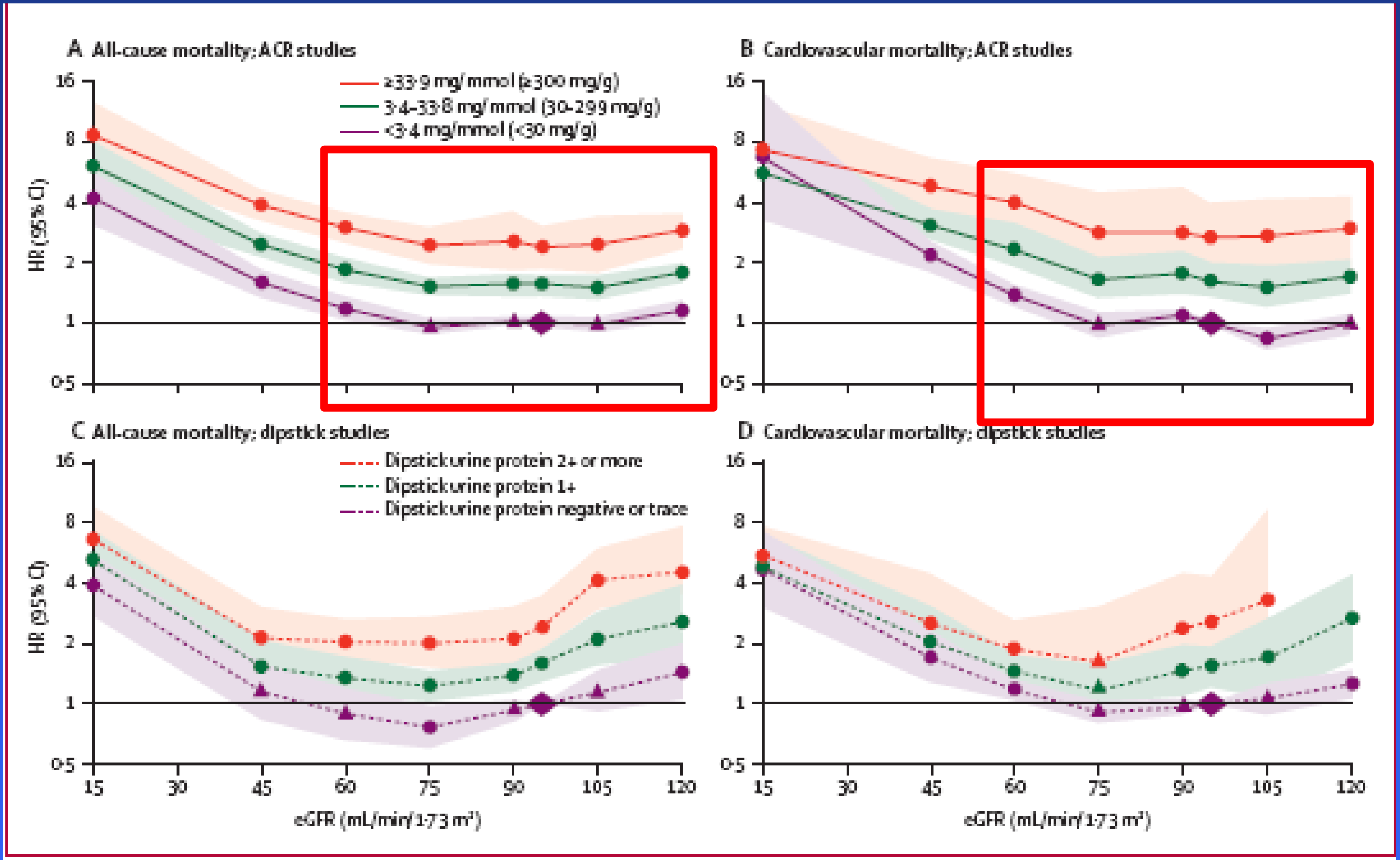

Figure 3: Hazard ratios and 95% CIs for all-cause and cardiovascular mortality according to spline estimated glomerular filtration rate (eGFR) and categorical albuminuria

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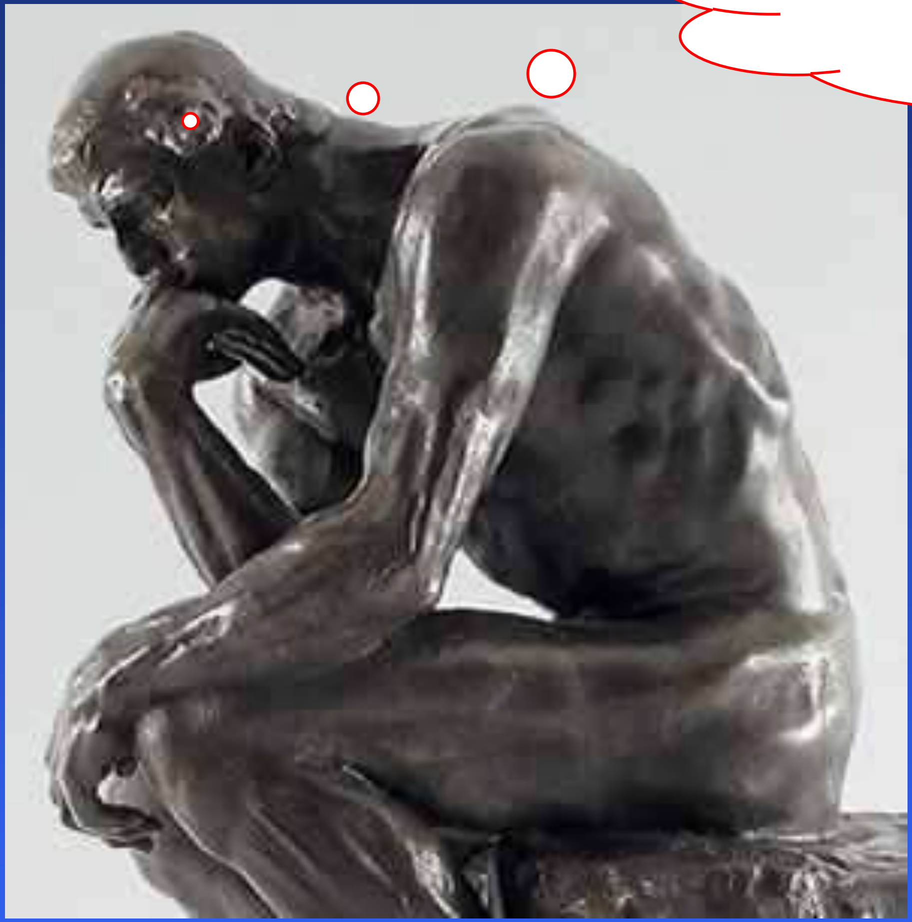
Lancet 2010

Sheffield Kidney Institute



WHAT IS THE EVIDENCE???

EVIDENCE
QUALITY
INTERPRETATION
USEFULNESS

Are Nephrologists capable of Critical Thinking?!

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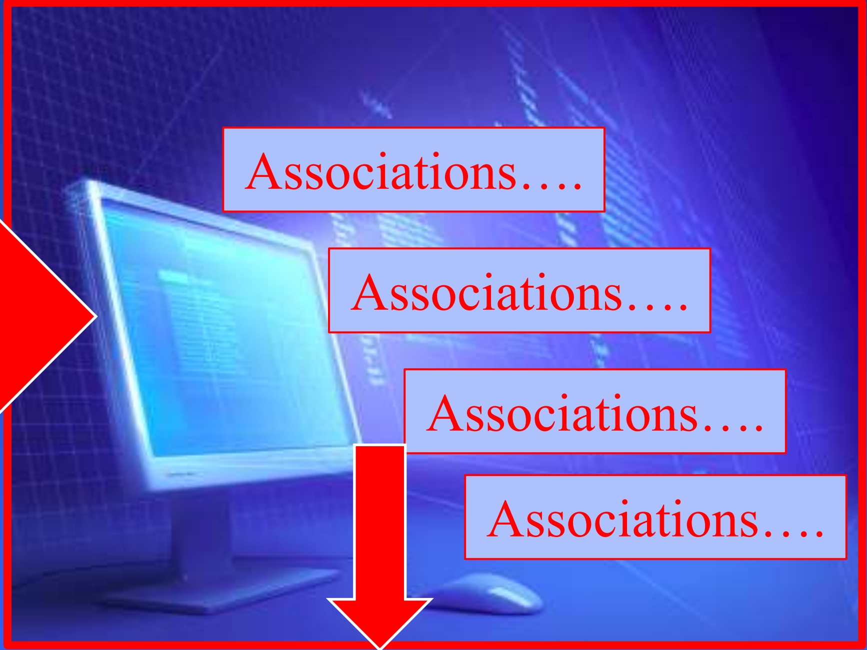
Global CKD Screening Programmes

CKD : Predictor of CVD Risk

Epidemiologists

Computerised Databases



CVD


Epidemiology
50%
15%
10
%
5%
CKD
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Table 2. Summary of the prevalence of CKD reported in high quality studies (%; 95% confidence interval)

Study ID	Measure of CKD	Prevalence (all)	Prevalence (male)	Prevalence (female)	Comment
Community-screening studies					
Chen *et al.* [27], China	Chinese 4v eGFR single sample	eGFR < 60: 3.2 (2.8–3.7) eGFR 30–59: 2.8e GFR 1–29: 0.3 eGFR < 15: 0.1	eGFR < 60: 4.1	eGFR < 60: 2.2	Stratified, multistage sampling, representative of the city of Guangzhou population (adults 20 years)
Coresh *et al.* [4], USA NHANES III	4v eGFR single sample	eGFR 15–59: 4.5 (4.1–4.9) eGFR 30–59: 4.3 (3.9–4.7) eGFR 15–29: 0.2 (0.14–0.26)	eGFR 15–59: 3.6 (3.0–4.3) eGFR 30–59: 3.4 (2.8–4.0) eGFR 15–29: 0.2 (0.10–0.30)	eGFR 15–59: 5.3 (4.4–6.2) eGFR 30–59: 5.1 (4.3–5.9) eGFR 15–29: 0.2 (0.10–0.30)	Standardized to US census population by age, sex and race (adults 20 years)
Coresh *et al.* [17], USA, NHANES III.	4v eGFR1999–2004 single sample.	eGFR 15–59: 8.1 (7.3–8.9) eGFR 30–59: 7.7 (7.0–8.4) eGFR 15–29: 0.35 (0.25–0.45)			Standardized to US census population by age, sex and race (adults 20 years)
Hallan *et al.* [31], Norway, HUNTII	4v eGFR single sample	eGFR < 60: 4.7			Standardized to Norwegian census population by age (adults 20 years)
Zhang *et al.* [55], China.	4v eGFR single sample	eGFR < 60: 1.7(1.2–2.1)	eGFR < 60: 1.4	eGFR < 60: 2.0	Representative sample of Beijing city (adults 18 years)
Community-screening studies: age restricted					
Chen *et al.* [37], China, InterAsia	4v eGFR single sample	eGFR < 60: 2.5 (2.1–2.9) eGFR 30–59: 2.4 (2.0–2.8) eGFR < 30: 0.1 (0.09–0.11)	eGFR < 60: 1.4 (0.9–1.9) eGFR 30–59: 1.2 (0.8–1.6); eGFR < 30: 0.2 (0.08–0.32)	eGFR < 60: 3.8 (3.1–4.5) eGFR 30–59: 3.7 (3.1–4.3) eGFR < 30: 0.1 (0.0–0.22)	Standardized to Chinese population by age, sex and geography (adults aged 35–74 years)
Perkovic *et al.* [45], Thailand, InterAsia	4v eGFR single sample	eGFR 15–59: 13.8 (10.9–16.7) eGFR 30–59: 13.2 (10.6–15.8) eGFR 15–29: 0.61 (0.29–0.93)	Stages 3–5: 11.6 (8.7–15.7) eGFR 30–59: 11.5 (8.6–14.4) eGFR < 30: 0.7 (0.11–1.3)	Stages 3–5: 15.7 (11.2–20.2) eGFR 30–59: 15.1 (11.0–19.2) eGFR < 30: 0.6 (0.21–0.99)	Standardized to the census population (adults 35 years)
Routine health care data					
John *et al.* [59], UK	Creatinine thresholds two samples	Creatinine threshold: 0.6	Creatinine > 180: 0.5	Creatinine > 135: 0.6	Percentage of the catchment area population identified by routine testing (adults 18 years)
Nissenson *et al.* [66], USA	Creatinine thresholds two samples	Creatinine threshold: 1.7	Creatinine > 124: 1.9	Creatinine > 106: 1.5	Based on percentage of those with two or more tests performed as part of routine practice, standardized by age and sex to US population (all ages)
Risch *et al.* [61], Liechtenstein	4veGFR single sample	eGFR < 60: 4.9 eGFR 30–59: 4.4 eGFR 15–29: 0.5 eGFR < 15: 0.1			Catchment area population denominator, proportions standardized to census demographics (adults ≥ 25 years)
Stevens *et al.* [65], USA	4veGFR two samples	Stages 3–5: 24.0			Percentage of those with two or more tests performed as part of routine practice (adults ≥ 40 years with high comorbidity)

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McCullough et al, 2012

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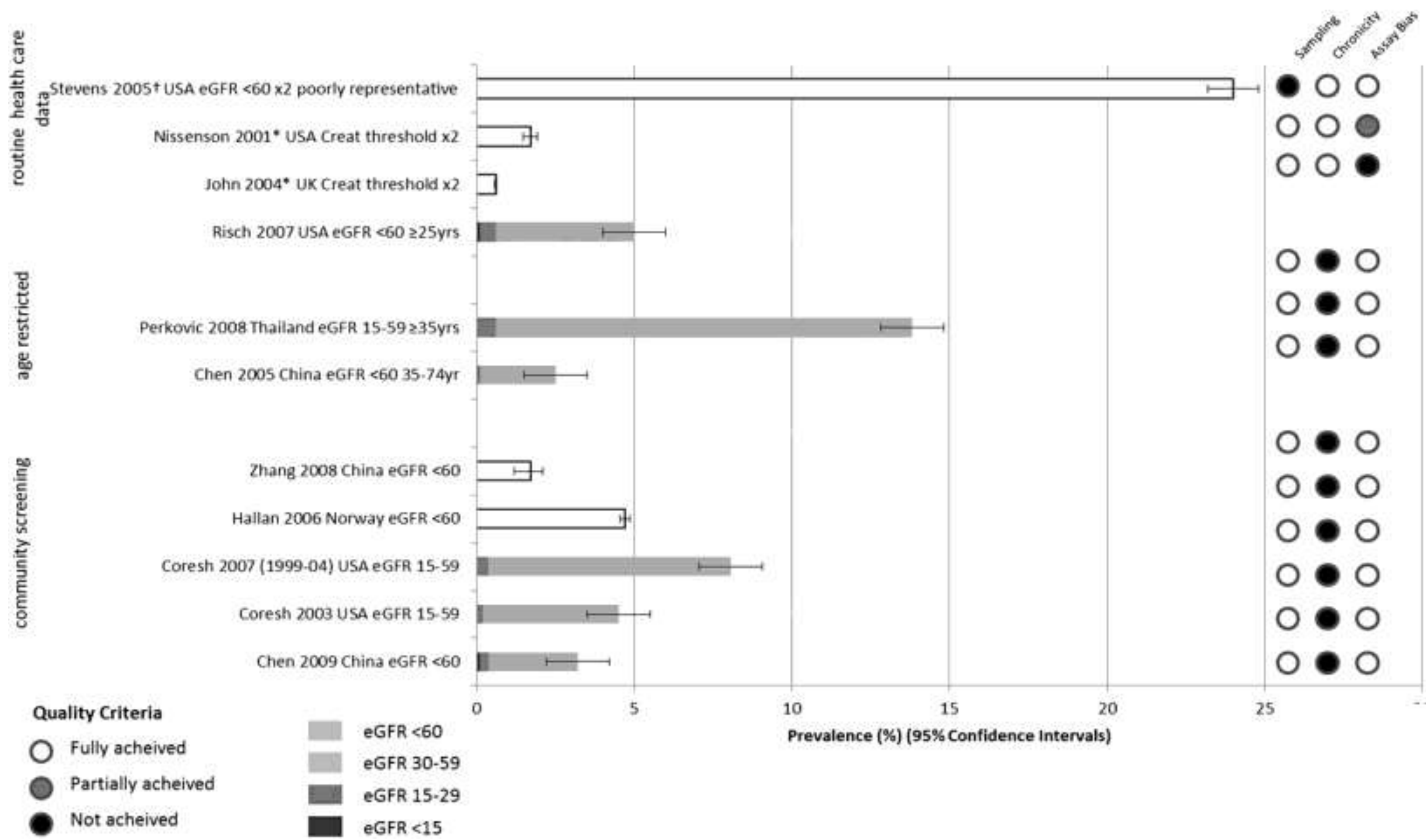

Fig. 4. Prevalence (95% confidence interval) of iKF reported in high quality studies.

Table 1. Description of studies examining CKD measures to improve CVD risk prediction

Author year	Population	Primary outcome	Model predictors	Added biomarkers	Original AUC	Change in AUC with biomarkers
Wang et al., 2006 [40]	Framingham Offspring study	Fatal and nonfatal MI, coronary insufficiency, CHF, stroke	Age, sex, DM, smoking status, BP categories, TC, HDL, BMI, creatinine	ACR, BNP	0.76	+0.01
Hallan et al., 2007 [10]	Population-based Norwegian study	Cardiovascular death (ICD-10 codes I10-I15, I20-I25, I44-I49, I50, I60-I69, I70-I77)	Age, sex, DM, smoking status, SBP, BP medication, TC, HDL, prevalent CVD	eGFR and ACR categories	Age <70 years 0.91 Age ≥70 years 0.76	Age <70 +0.002 Age ≥70 +0.01
Olsen et al., 2007 [56]	Population-based Danish study	Cardiovascular death, non-fatal MI, stroke	Age, sex, DM, smoking status, SBP, LDL, heart rate, glucose, LVEF, prior MI, prior stroke	ACR, hsCRP, NT-proBNP	0.82	+0.01 (ACR) +0.02 (all 3 biomarkers)
Weiner et al., 2007 [46]	Pooled from 2 population-based US studies, 1 study with adults >65 years age	CHD death, nonfatal MI	Age, sex, DM, smoking status, BP categories, TC, HDL	eGFR <60	White men 0.74 AA men 0.64 White women 0.78 AA women 0.75	White men +0.002 AA men –0.002 White women +0.001 AA women +0.004
Zethelius et al., 2008 [41]	Community-based cohort of elderly Swedish men (subsample without CVD)	Cardiovascular death (ICD-10 codes I00-I99)	Age, DM, smoking status, SBP, BP medication, TC, HDL, cholesterol medication, BMI	Cystatin C, troponin, CRP, NT-proBNP	0.69	+0.01 (cystatin C) +0.06 (all 4 biomarkers)
Shlipak et al., 2008 [47]	Adults with pre-existing CHD	CHD death, nonfatal MI, stroke	Age, sex, race, DM, smoking status, HTN, BMI, creatinine, aspirin use, LVEF <50, prior MI, prior stroke	ACR, CRP, NT-proBNP	0.73	+0.04 (all 3 biomarkers)
Ito et al., 2010 [48]	Population-based multiethnic US study without clinical CVD	CVD death, resuscitated cardiac arrest, nonfatal MI, stroke, angina, PAD, CHF	Age, sex, DM, smoking status, SBP, BP medication, TC, HDL, cholesterol medication, BMI	Creatinine or cystatin C	0.72	–0.01 (creatinine) +0.02 (cystatin C)

DM = Diabetes mellitus; TC = total cholesterol; HDL = high-density cholesterol; LDL = low-density cholesterol; BMI = body mass index; BNP = brain natriuretic peptide; PAD = peripheral arterial disease; CHF = congestive heart failure; ICD = International Statistical Classification of Diseases; LVEF = left ventricular ejection fraction; hsCRP = high-sensitivity C-reactive protein; NT-proBNP = N-terminal pro-brain natriuretic peptide.

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Chang and Kramer, 2011

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REVIEW | 2013 | Annals of Internal Medicine

Risk Prediction Models for Patients With Chronic Kidney Disease

A Systematic Review

Navdeep Tangri, MD, PhD; Georgios D. Kitsios, MD, PhD, MS; Lesley Ann Inker, MD, MS; John Griffith, PhD; David M. Naimark, MD, MSc; Simon Walker, BSc(Hons); Claudio Rigatto, MD, MSc; Katrin Uhlig, MD, MS; David M. Kent, MD, MS; and Andrew S. Levey, MD

Figure. Risk of bias and clinical usefulness of prediction models.

+ = High risk of Bias

Outcome	Study	Study Participation	Study Attrition	Prognostic Factor Selection	Prognostic Factor Measurement	Outcome Measurement	Analysis	Reporting of Model Performance	Clinical Utility	Clinical Usability
Kidney failure	Desai et al, 2011 (20)	+	–	+	?	+	–	+	–	–
	Dimitrov et al, 2003 (14)	+	?	+	?	–	?	+	–	–
	Goto et al, 2009 (18)	+	+	?	?	+	+	+	–	–
	Johnson et al, 2008 (17)	+	?	+	+	+	+	+	+	+
	Keane et al, 2006 (15)	+	?	+	?	+	+	–	–	–
	Landray et al, 2010 (19)	+	+	+	+	+	+	+	–	+
	Tangri et al, 2011 (7)	+	?	+	+	+	+	+	+	+
	Wakai et al, 2006 (16)	+	+	+	+	+	+	+	–	–
All-cause mortality	Berthoux et al, 2011 (25)	+	?	?	+	+	+	–	–	–
	Desai et al, 2011 (20)	+	–	+	?	+	–	+	–	–
	Johnson et al, 2007 (24)	+	+	+	+	+	+	+	–	–
	Keane et al, 2006 (15)	+	?	+	?	+	+	–	–	–
	Landray et al, 2010 (19)	+	+	+	+	+	+	+	–	+
Cardiovascular events	McMurray et al, 2011 (23)	+	?	+	?	?	+	+	–	–
	Shlipak et al, 2005 (21)	+	?	+	+	+	+	+	–	–
	Weiner et al, 2007 (22)	+	?	?	?	+	+	+	–	–

Bias | Usefulness

– = Not Clinically Useful

Risk-of-bias items were evaluated as low risk (–), high risk (+), or unknown risk (?). Clinical usefulness was evaluated as yes (+) or no (–).

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Tangri, Levey et al 2013

Models predicting CVD and all cause Mortality:

1. Did NOT provide a decision aid that could be used at the bedside

1. None were validated in our external population

Review 2013 Annals of Internal Medicine

Risk Prediction Models for Patients With Chronic Kidney Disease

A Systematic Review

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epidemiologic research. Whether the addition of proteinuria or such newer biomarkers as cystatin C or fibroblast growth factor 23 will further aid risk stratification for CVD in patients with CKD is unknown and should be investigated (39, 40).

Conclusion: Accurate, externally validated models for predicting risk for kidney failure in patients with CKD are available and ready for clinical testing. Further development of models for cardiovascular events and all-cause mortality is needed.

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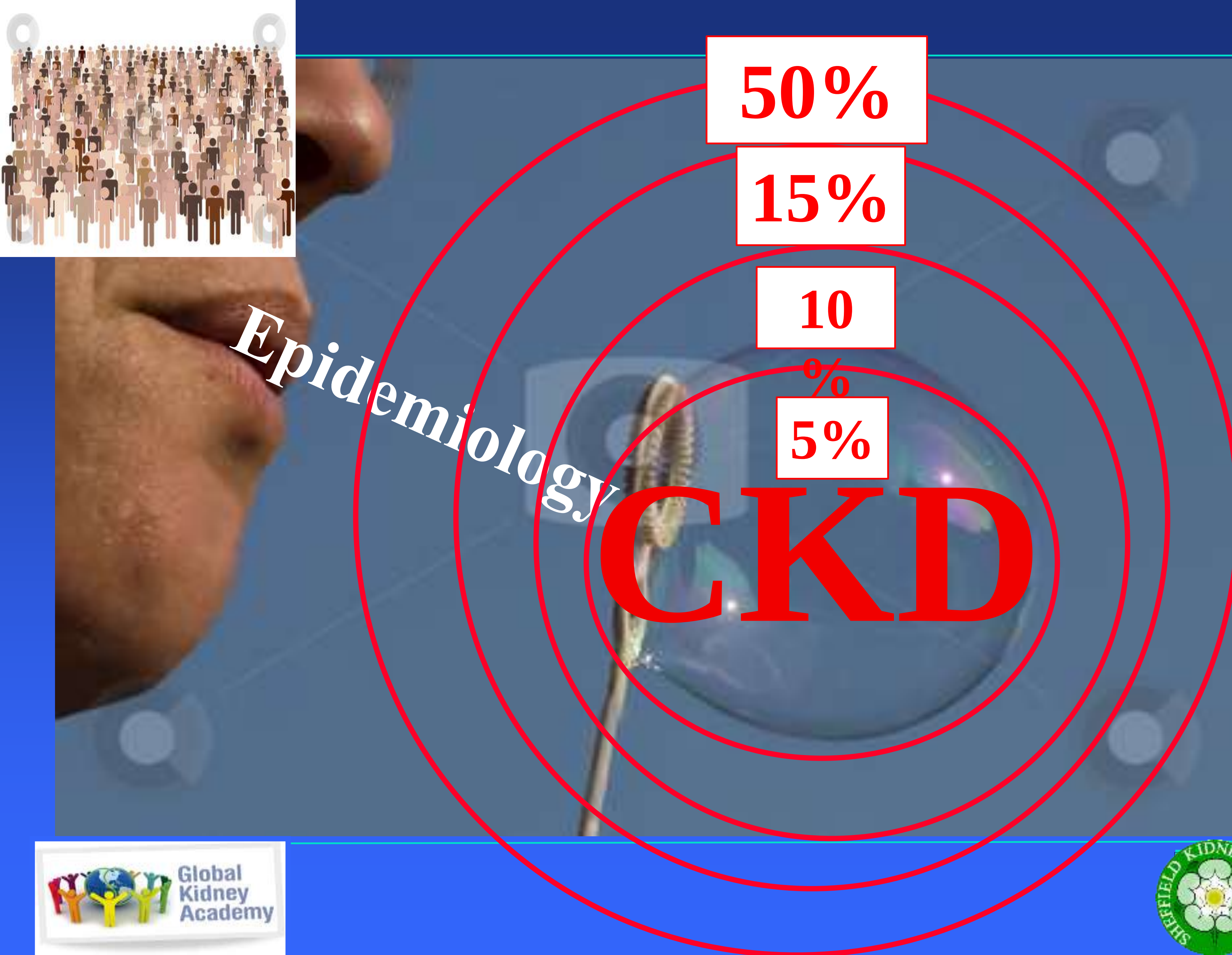
cCKD = C-K-D

Older People with CVD = C-K-D



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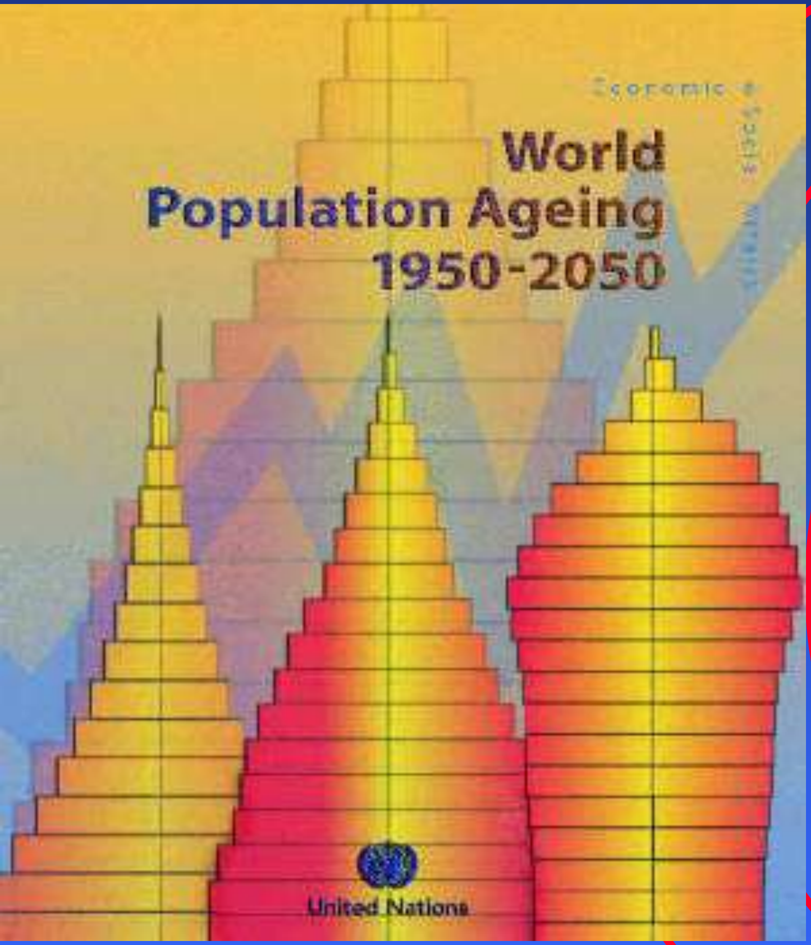

25%

15%

10 %

5%

People >60!

Further Discussion…

OnlineAcademy

GlobalKidneyAcademy

http://www.gkaonlineacademy.com/forum

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